Amendment To The Claims

Listing of the Claims

- 1. (Currently amended) A mouse, comprising at least one cell that comprises a human chromosome fragment that is not integrated into the mouse cell genome, wherein the human chromosome fragment expresses at least one human cytochrome <u>CYP3A4 family</u> P450 3A family gene.
 - 2. (Canceled)
- 3. (Previously Presented) The mouse of claim 1, wherein said human chromosome fragment is introduced by microcell fusion using the chromosome fragment.
- 4. (Previously Presented) The mouse of claim 3, wherein the mouse is a chimeric mouse.
- 5. (Currently Amended) A mouse, which is obtained by mating a wild-type mouse of the same kind as the mouse of claim 4 with the mouse of claim 4 and which harbors a human chromosome fragment containing a human cytochrome CYP3A4 family P450 3A family gene that is not integrated into the mouse cell genome.
- 6. (Withdrawn) A nonhuman mammalian according to claim 1, wherein a cytochrome P450 gene inherent to said nonhuman mammalian that is a homolog of said human cytochrome P450 gene has been disrupted and expression of the inherent gene has been reduced or lost.
 - 7. (Canceled)
 - 8. (Canceled)
- 9. (Currently Amended) A cell, organ, or tissue obtained from the <u>liver or small</u> intestine of the mouse of claim 1, wherein the cell or tissue and which is capable of expressing the human cytochrome <u>CYP3A4 family P450 3A family</u> gene.

- 10. (Withdrawn) A method for preparing a physical map for determining arrangement of mouse Cyp3a genes on a chromosome, comprising the steps of: (a) screening a mouse BAC library by PCR or hybridization using PCR primers or a probe for hybridization for specifically detecting each mouse Cyp3a genes; (b) repeating a cycle of screening the BAC library several times to prepare a BAC contig, the cycle comprising determining a terminal nucleotide sequence of the BAC clones selected in the above step and preparing a primer or a probe based on the nucleotide sequence; and (c) determining both ends of a Cyp3a gene cluster by preparing a full-length cDNA probe of an unprescribed mouse Cyp3a gene and performing hybridization of the above-mentioned BAC contig using the probe under the gentle conditions.
- 11. (Withdrawn) A physical map which can be prepared by the method according to claim 10 and having elucidated the arrangement of the mouse Cyp3a genes on the chromosome.
- 12. (Withdrawn) A method of preparing a targeting vector for deleting mouse Cyp3a genes, comprising cloning a genome DNA corresponding to respective terminals of a mouse Cyp3a gene cluster based on the physical map according to claim 11 and inserting each of the obtained cloned fragments into a vector containing a loxP sequence, which is a recognition sequence of recombinase Cre derived from bacteriophage P1.
- 13. (Withdrawn) A pair of targeting vectors for deleting mouse Cyp3a genes that can be prepared by the method according to claim 12, wherein the respective vectors are to be incorporated in a mouse chromosome and only when said enzyme Cre is present, homologous recombination occurs between the loxP sequences, thereby deleting the whole Cyp3a gene cluster.
- 14. (Withdrawn) A method of deleting Cyp3a genes of a mouse cell, comprising the steps of introducing the vector according to claim 13 into a cell retaining pluripotency of a mouse and expressing enzyme Cre.
- 15. (Withdrawn) A mouse cell that can be prepared by the method according to claim 14, being deficient in Cyp3a genes and retaining pluripotency.

- 16. (Withdrawn) A method of preparing a knockout mouse deficient in Cyp3a genes, comprising the step of differentiating the mouse cell according to claim 15.
- 17. (Withdrawn) A chimeric mouse or a progeny thereof prepared by the method according to claim 16, being deficient in Cyp3a genes.
- 18. (Withdrawn) A mouse or a progeny thereof deficient in Cyp3a genes, obtained by mating the chimeric mouse according to claim 17 or a progeny thereof with a wild-type mouse.
- 19. (Withdrawn) A tissue derived from the chimeric mouse according to claim 16 or a progeny thereof or the chimeric mouse according to claim 17 or a progeny thereof.
- 20. (Withdrawn) A cell derived from the chimeric mouse according to claim 16 or a progeny thereof or the chimeric mouse according to claim 17 or a progeny thereof.
- 21. (Withdrawn) A mouse or a progeny thereof obtained by mating the mouse according to claim 8 or a progeny thereof with the chimeric mouse according to claim 17 or a progeny thereof, or the mouse according to claim 18 or a progeny thereof, the mouse or a progeny harboring a human chromosome containing human P450 genes and being deficient in mouse Cyp3a genes.
- 22. (Withdrawn) A method of producing biologically active human cytochrome P450, comprising the steps of cultivating an individual, tissue or cell of the mouse according to claim 8 or a progeny thereof, expressing the human cytochrome P450 genes harbored therein to produce biologically active human cytochrome P450, and recovering the human cytochrome P450.
- 23. (Withdrawn) A method of producing biologically active human cytochrome P450, comprising the steps of cultivating an individual, tissue or cell of the mouse according to claim 21 or a progeny thereof, expressing the human cytochrome P450 genes harbored therein to produce biologically active human cytochrome P450, and recovering the human cytochrome P450.

- 24. (Withdrawn) A method of examining pharmacological effect and/or metabolism of a drug, comprising the step of administering the drug to an individual, tissue or cell of the mouse according to claim 8 or a progeny thereof or the mouse according to claim 21 or a progeny thereof.
- 25. (Currently Amended) The mouse according to claim 1, wherein the expression of the human cytochrome <u>CYP3A4 family P450 3A family gene</u> is regulated by the expression control region of the human cytochrome <u>CYP3A4 P450 3A</u> gene and is induced by a compound which induces the expression of a human cytochrome <u>CYP3A4 family P450 3A family gene</u>.